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AN - 1995-366914 [48]
AP - CN19930112451 19930531
CPY - UYSH-N
DC - B01 B04
FS - CPI
IC - C07J71/00
IN - HU Y; XIA Z; YI N
MC - B04-A07E B14-J02
PA - (UYSH-N) UNIV SHANGHAI NO 2 MEDICAL
PN - CN1096031 A 19941207 DW199548 C07J71/00 000pp
PR - CN19930112451 19930531
XA - C1995-159732
XIC - C07J-071/00
AB - CN1096031 The saponin of wind-weed is new.
- USE - The saponin has bidirectional adjusting function against two kinds of receptor, and is different from excitant or antagonist in Western medicine.
- ADVANTAGE - The saponin does not cause the "rebound" phenomenon on withdrawal. The production is low cost, high yield and convenient.
IW - MEDICINE REGULATE BETA ADRENERGIC CHOLINERGIC RECEPTOR
IKW - MEDICINE REGULATE BETA ADRENERGIC CHOLINERGIC RECEPTOR
INW - HU Y; XIA Z; YI N
NC - 001
OPD - 1993-05-31
ORD - 1994-12-07
PAW - (UYSH-N) UNIV SHANGHAI NO 2 MEDICAL
TI - Medicine regulating beta adrenergic and M-cholinergic receptor

[redacted] !
CN1993-011245 1

1/1 - (C) FILE HCAPLUS
STN CA Caesar accession number : 1802
AN - 1995:881491 HCAPLUS
DN - 123:266081
TI - Extraction of .beta.-adrenergic receptor- and M cholinergic receptor-regulating (.beta.,5.beta.,25s)-spirostan-3-ol from Anemarrhena asphodeloides Bunge
IN - Yi, Ningyu; Xia, Zongqin; Hu Ya, Er
PA - Shanghai No. 2 Medical University, Peop. Rep. China
SO - Faming Zhuanli Shenqing Gongkai Shuomingshu, 5 pp.
CODEN: CNXXEV
DT - Patent
LA - Chinese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PN -	CN1096031	A	19941207	CN 1993-112451	19930531
	CN1033754	B	19970108		

AB - .beta.-Adrenergic receptor- and M cholinergic receptor-regulating (3.beta.,5.beta.,25s)-spirostan-3-ol (I) was extd. from A. asphodeloides Bunge by pulverizing the material, soaking in warm water, treating with 3.5 vols. of 3% H2SO4 at 0.7-1.2 kgf/cm2, hydrolyzing at 115-122.degree. for 6-10h, filtering, washing to neutral pH, drying, extg. with Et acetate for 2 times, and crystg. with acetone . The method was simple and the yield was high.

IT - 126-19-2P
RL: BAC (Biological activity or effector, except adverse); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(extn. of .beta.-adrenergic receptor- and M cholinergic receptor-regulating (3.beta.,5.beta.,25s)-spirostan-3-ol from Anemarrhena asphodeloides Bunge)
RN - 126-19-2 HCAPLUS
CN - Spirostan-3-ol, (3.beta.,5.beta.,25S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
[--00001747]

[19]中华人民共和国专利局

[11] 公开号 CN 1096031A

[12] 发明专利申请公开说明书

[21]申请号 93112451.4

[51]Int.Cl⁵
C07J 71/00

[43]公开日 1994 年 12 月 7 日

[22]申请日 93.5.31

[71]申请人 上海第二医科大学
地址 200025上海市重庆南路280号
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[74]专利代理机构 上海高校专利事务所
代理人 陈悦昌 曹羽

说明书页数: 3 附图页数:

[54]发明名称 对β肾上腺素受体和M胆碱受体有双向调节作用的药物及其制法

[57]摘要

本发明是一种对β肾上腺素受体和M胆碱受体有双向调节作用的药——如母菊苷元及其制法。它具有对两种受体有双向调节作用的特殊优点，并且不同于西药中的激动剂或拮抗剂，不存在停药"反跳"现象。其制造工艺亦具有成本低，简单易，操作方便，适用于大规模生产等特点。

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[71]申请人 上海第二医科大学
地址 200025上海市重庆南路280号
[72]发明人 易宁育 王宗勤 胡益儿

[74]专利代理机构 上海高校专利事务所
代理人 陈世昌 曹羽

说明书页数: 3 附图页数:

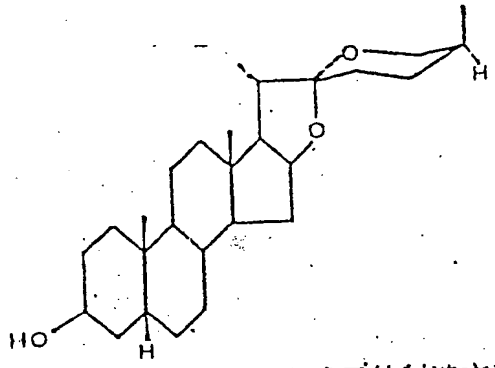
[54]发明名称 对β肾上腺素受体和M胆碱受体有双向调节作用的药物及其制法

[57]摘要

本发明是一种对β肾上腺素受体和M胆碱受体有双向调节作用的药——加母皂苷元及其制法。它具有对两种受体有双向调节作用的特殊优点，并且不同于西药中的激动剂或拮抗剂，不存在停药"反跳"反应。其制造工艺亦具有成本低，得率高，操作简便，适用于大规模生产等特点。

权　利　要　求　书

1、一种对β肾上腺素受体和M胆碱受体有双向调节作用的药物——知母皂甙元，其特征在于它的结构式为



2、如权利要求1所述的知母皂甙元的制造方法，其特征在于：

a、将知母切碎，烘干、打粉，以温水浸泡；

b、加3.5倍体积的3%H_2SO_4在0.7—1.2kgf/cm²的压力下，在115—122℃水解6—10小时，过滤后水洗至中性、烘干；

c、以乙酸乙酯回流，经2次提取，再以丙酮重结晶而得。

说　　明　　书

对β肾上腺素受体和M胆碱受体有双向调节作用的药物及其制法

本发明揭示一种对β肾上腺素受体和M胆碱受体有双向调节作用的药物——知母皂甙元及其制法，属于药物制造领域。

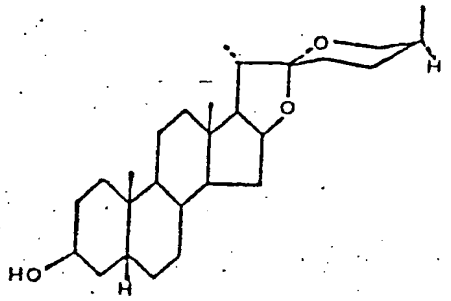
细胞受体的生物学和医学意义越来越为人们所重视，它和中枢神经系统的活动、神经内分泌对细胞的调节作用，药物作用，免疫调控等都有密切关系。细胞受体和临床的关系也日益为人们所认识。国际上受体药的研究发展很快，但主要是合成药，而且基本上是与受体起结合反应的激动剂或拮抗剂。这些药的作用属对症性，它们的共同缺点是：副作用较多，作用时间短，而且可能出现停药"反跳"现象。

本发明的目的在于：提出一种对β肾上腺素受体和M胆碱受体有调整作用的药及其适于大规模生产，操作简便，成本低，得率高的制法。

本发明的目的是通过下述技术方案来实现的：

首先将知母(Anemarrhena asphodeloides Bunge)切碎，烘干、打粉，以温水浸泡，加3.5倍体积的3%H_2SO_4，在0.7—

1.2Kgf/cm²的压力下，温度为115℃－122℃水解6小时；过滤后水洗至中性，烘干；再以乙酸乙酯回流，经两次萃取，最后以丙酮重结晶，得到纯度为95%以上的知母皂甙元(洋菝葜皂甙元)——(3β，5β，25s)－Spironslan－30 l 。结构为：



本发明的明显特点是：

1、对病理性升高的内脏(包括脑)及外周血淋巴细胞的β肾上腺素受体数，以及β肾上腺素受体激动剂引起的血浆CAMP过度升高，有明显的下调作用，使这些变化恢复至正常。

2、对病理性降低的内脏(包括脑)M胆碱受体有明显的上调作用，使之恢复到接近正常。

3、对自然衰老动物降低的脑M受体有明显的上调作用，同时显著延长其平均寿命。

4、与西药中的激动剂或拮抗剂不同，并非与受体的结合位点起结合反应，而是调节受体分子的生成速率和降解速率，因此不存在激动剂或拮抗剂的停药反跳副作用。

5、制造方法操作简便、成本低，产率高，适合于工业化生产。

下面结合实施例，对本发明作进一步描述：

实施例1：将100g知母切碎打粉，温水浸泡，再加以3.5倍体积的3%H_2SO_4，在0.7Kgf/cm² 115℃下酸解8小时，残渣水洗至中性，80℃烘干；再以乙酸乙酸回流萃取，回收溶剂，残渣用丙酮重结晶两次，得95%以上的知母皂甙元(得率1.2%)。

实施例2：将300g知母切碎，打粉，温水浸泡，再加以3.5倍体积的3%H_2SO_4，在1.05Kgf/cm²，121℃，下酸解10小时残渣水洗至中性，80℃烘干，乙酸乙酯回流萃取，回收溶剂，残渣用丙酮重结晶两次，得95%以上的知母皂甙元(得率2.0%)。

(19) The Patent Bureau, P.R. China

(11) Opening No. CN 1096031A

(12) Opening Exposition of Application for Invention Patent

PRC

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(51) Int.Cl[5]

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(22) Date of Application: 31 May 1993

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Address: 280 Chong-Qing Nan Lu
Shanghai 200025

(72) Inventors: Yi Ning-Xiao, Xia Zong-Qin, Hu Ya-Er

(74) Patent Agent:
Shanghai Universities/Colleges Patent Agency

Agents: Su Shi-Hao, Shu Yu

Pages of Exposition: 3, Pages of Diagram:

(54) Title of Innovation: A drug which has two-way regulatory effects on β-adrenergic and M-cholinergic receptors, and its manufacturing technique.

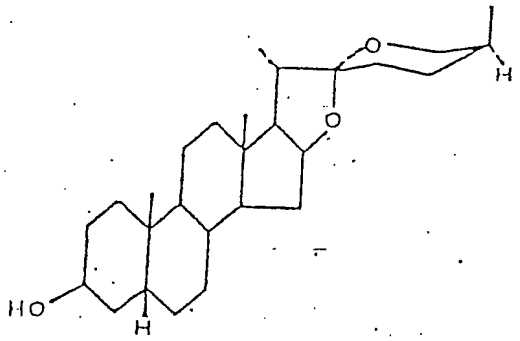
(57) Abstract: This invention is Zhi Mu Sarsasapogenin (ZMS) and its manufacturing method. ZMS is a drug which has two-way regulatory effects on β-adrenergic and M-cholinergic receptors. The drug possesses a special advantage of having two-way regulatory effects on the two types of receptor. Unlike an agonist or antagonist in Western medicine, it does not result in a phenomenon of "rebound" or "recurrence" after its administration is stopped. Its manufacturing technique has such advantages as low costs, high rate of output, easy to operate, and suitable for large-scale production.

(BJ) No. 1456

Claims

1. Zhi Mu Sarsasapogenin (ZMS)- a drug which has two-way regulatory effects on β-adrenergic and M-cholinergic receptors

Its features lie in its structure:



2. The manufacturing procedure of ZMS as described in Claim 1.

Features of the manufacturing procedure are:

a. Anemarrhena asphodeloides Bunge is sliced, dried and ground into powder, and then soaked in lukewarm water.

b. 3.5 times of 3% H_2SO_4 is added, and hydrolysed for 6-10 hours under 115-122 °C and 0.7-1.2 kgf/cm. The solution is filtered, and the residue is washed until it becomes neutral and then dried.

c. The dried residue is extracted twice under reflux with Ethyl Acetate, and then re-crystallised using acetone.

Expositions

A drug which has two-way regulatory effects on β-adrenergic and M-cholinergic receptors, and its manufacturing technique

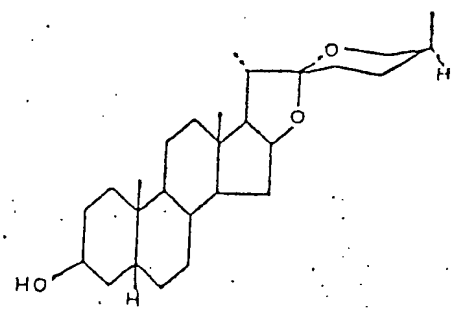
This invention has revealed a drug which has two-way regulatory effects on β-adrenergic and M-cholinergic receptors - Zhi Mu Sarsasapogenin, and its manufacturing technique. The invention belongs to the area of drug manufacturing.

Increasing attention has been paid to the biological and medical significance of the cell receptor. It has close relations with activities of the central nervous system, regulatory effects of nervous endocrine on cells, drug effects and immune adjustment. The relationship between the cell receptor and clinic has also been gradually recognised. Quick progress has been made in receptor drug research in the world. However, these receptor drugs are mainly synthetic. They are basically agonists or antogonists which exert combined effects via binding themselves with receptors. Their common shortcomings include various side effects, short period of action, and possible phenomenon of "rebound" or "recurrence" when drug administration is stopped.

The objective of this invention is to present a drug which has regulatory effects on adrenergic and M-cholinergic receptors, and the manufacturing procedure which is suitable for large-scale production, easy to operate, low in costs, and high in the rate of output.

The objective is realised via the following technical scheme:

Anemarrhena asphodeloides Bunge is sliced, dried and ground into powder, and then soaked in lukewarm water. 3.5 times of 3% H_2SO_4 is added, and hydrolysed for 6 hours under 0.7-1.2 kgf/cm and 115-122 ^{0}C. The solution is filtered, and the residue is washed until it becomes neutral and then dried. The dried residue is extracted twice under reflux with Ethyl Acetate, and finally re-crystallised using acetone to obtain over 95% Zhi Mu Sarsasapogenin - (3β, 5β, 25s) - Spironstan -301. Its structure is as follows:



The distinct features of this invention are:

1. Observable downward regulation towards normalisation of a pathological rise in number of β-adrenergic receptors of internal organs (including brain) and lymphocyte of peripheral blood streams, and of a rise in plasma CAMP caused by β-adrenergic receptor agonists.

2. Observable upward regulation towards near normalisation of a pathological fall in M-cholinergic receptors of internal organs (including brain).

3. Observable upward regulation of a fall in in M-cholinergic receptors of animal brain caused by natural ageing and observable prolongation of animal life

4. Unlike an agonist or antogonist in Western medicine, ZMS does not occupy the binding sites of receptors to exert combined effects. Rather, it regulates speeds of the formation and disintegration of receptor molecules. Thus, it has no "rebound" or "recurrence" effects associated with agonists or antogonists.

5. The manufacturing procedure is simple, its cost is low, and the rate of output is high. ZMS is suitable for industrial production.

The invention is further described using the following examples:

Example 1:
100 gram of Anemarrhena asphodeloides Bunge is sliced, ground into powder, and soaked in lukewarm water. 3.5 times of 3% H_2SO_4 is added, and acidolysed for 8 hours under 0.7 kgf/cm and 115 °C. The residue is washed until it becomes neutral, dried at 80 °C, and then extracted with Ethyl Acetate under reflux. The reagent is retrieved, and the residue is re-crystallised twice using acetone to obtain over 95% Zhi Mu Sarsasapogenin (the rate of output is 1.2%).

Example 2:
300 gram of Anemarrhena asphodeloides Bunge is sliced, ground into powder, and soaked in lukewarm water. 3.5 times of 3% H_2SO_4 is added, and acidolysed for 10 hours under 1.05 kgf/cm and 121°C. The residue is washed until it becomes neutral, dried at 80C, and then extracted with Ethyl Acetate under reflux. The reagent is retrieved, and the residue is re-crystallised twice using acetone to obtain over 95% Zhi Mu Sarsasapogenin (the rate of output is 2.0%).